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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/854,825	05/12/1997	FRANCIS V. CHISARI	329368-101CO	9805

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EXAMINER	
PARKIN, JEFFREY S	

ART UNIT	PAPER NUMBER
1648	32

DATE MAILED: 05/07/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application N .	Applicant(s)	
	08/854,825	CHISARI ET AL.	
	Examiner	Art Unit	
	Jeffrey S. Parkin, Ph.D.	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the corresp ndence address --

Peri d for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 03 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 February 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disp sition of Claims

4)☐ Claim(s) _____ is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *67-97* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ ~~Notice of References Cited (PTO-892)~~
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *29* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

Response to Amendment

Status of the Claims

1. Acknowledgement is hereby made of receipt and entry of the amendment filed 06 February, 2003, wherein claims 67 and 97 were amended. Claims 67-97 are currently under examination.

Information Disclosure Statement

2. The information disclosure statement filed 06 February, 2003, has been placed in the application file and the information referred to therein has been considered.

35 U.S.C. § 112, First Paragraph

3. The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 67-97 stand rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. *In re Rasmussen*, 650 F.2d 1212, 211 U.S.P.Q. 323 (C.C.P.A. 1981). *In re Wertheim*, 541 F.2d 257, 191 U.S.P.Q. 90 (C.C.P.A. 1976). The claims are directed toward HCV CTL epitopes carrying one to two amino acid additions, deletions, or substitutions. Immunogenic and pharmaceutical compositions comprising the claimed peptides, as well as, various methods of use are also claimed. Additional

embodiments are also directed toward conjugates comprising the peptides of interest.

The written description requirement under Section 112, first paragraph, stipulates that the claimed subject matter must be supported by an adequate written description that is sufficient to enable anyone skilled in the art to make and use the invention. The courts have decided that the specification must demonstrate that the inventor had possession of the claimed invention as of the filing date relied upon. Although the claimed subject matter need not be described identically, nonetheless, the disclosure relied upon must convey to those skilled in the art that applicants had invented the subject matter claimed. *Ralston Purina Company* v. *Far-Mar-Co., Inc.*, 227 U.S.P.Q. 177 (C.A.F.C. 1985). *In re Wilder, et al.*, 222 U.S.P.Q. 369 (C.A.F.C. 1984). *In re Wertheim, et al.*, 191 U.S.P.Q. 90 (C.C.P.A. 1976). *In re Blaser, Germscheid,* and *Worms,* 194 U.S.P.Q. 122 (C.C.P.A. 1977). *In re Driscoll,* 195 U.S.P.Q. 434 (C.C.P.A. 1977). *Utter* v. *Hiraga,* 6 U.S.P.Q.2d 1709 (C.A.F.C. 1988). *University of California* v. *Eli Lilly,* 119 F.3d 1559, 43 U.S.P.Q.2d 1398 (Fed. Cir. 1997). *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.,* 18 U.S.P.Q.2d 1016-1031 (C.A.F.C. 1991). *Fiers v. Sugano,* 25 U.S.P.Q.2d 1601-1607 (C.A.F.C. 1993). *In re Bell,* 26 U.S.P.Q.2d 1529-1532 (C.A.F.C. 1993). *In re Deuel,* 34 U.S.P.Q.2d 1210-1216 (C.A.F.C. 1995). Moreover, the courts have decided repeatedly that the inventor must clearly and unambiguously identify the salient characteristics and properties of any given claimed chemical compound, particularly as it applied to nucleic acids and peptides (*University of California* v. *Eli Lilly,* 119 F.3d 1559, 43 U.S.P.Q.2d 1398 (Fed. Cir. 1997); *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.,* 18 U.S.P.Q.2d 1016-1031 (C.A.F.C. 1991); *Fiers v. Sugano,* 25 U.S.P.Q.2d 1601-1607 (C.A.F.C. 1993); *In re Bell,* 26 U.S.P.Q.2d 1529-1532 (C.A.F.C. 1993); *In re Deuel,* 34

U.S.P.Q.2d 1210-1216 (C.A.F.C. 1995)). Thus, it is not sufficient to simply provide a vague reference to the biological activity of any given amino acid sequence or some generic method of obtaining it.

However, the skilled artisan, upon perusal of the disclosure would not accept the finding that applicants were in possession of the various peptidic variants currently encompassed by the claim language. The disclosure provides a small number of well-characterized HCV CTL epitopes (e.g., see SEQ ID NOS.: 1-3, 26, 34, 35, and 42). However, there are a number of deficiencies that clearly fail to place the applicants in possession of the claimed peptidic variants. First, the disclosure fails to provide sufficient guidance pertaining to the molecular determinants modulating the CTL-like properties of any given peptide. The disclosure fails to identify those portions of any given peptide that are critical for the retention of HCV CTL activity. Second, the disclosure fails to provide sufficient guidance pertaining to acceptable amino acid additions, substitutions, and deletions that will result in retention of the desired HCV CTL epitope. Thus, it is not clear from reviewing the specification which of the many possible amino acid changes are acceptable. Third, the prior art teaches that single amino acid changes, as well as, the addition or deletion of flanking regions, can influence the immunological properties of any given CTL epitope in an unpredictable manner (Smith *et al.*, 1997; Bertoletti *et al.*, 1994; Johnson *et al.*, 1992; Couillin *et al.*, 1995; and, Hahn *et al.*, 1992; Del Val *et al.*, 1991; Hahn *et al.*, 1992; and, Eisenlohr *et al.*, 1992). Moreover, as previously noted, the art teaches that the mere presence of an MHC class I binding motif in a peptide is not sufficient to confer binding to the appropriate class I molecule (Nayersina *et al.*, 1993; Bertoletti *et al.*, 1994; Couillin *et al.*, 1995; and, Eisenlohr *et al.*, 1992). Finally, as previously noted, the art

teaches that the capacity of a putative CTL epitope to bind to a class I molecule does not mean that the epitope will be immunogenic (Nayersina *et al.*, 1993; Couillin *et al.*, 1995; and, Eisenlohr *et al.*, 1992). The specification is silent concerning these caveats. Thus, the skilled artisan would reasonably conclude that applicants were not in possession of the claimed invention at the time of filing and are attempting to capture subject matter to which they are clearly not entitled.

Applicants traverse and submit that adequate written support exists for the limitations pertaining to the relative amount of sequence variability claimed. Applicants' arguments are not relevant to the rejection previously set forth under this statute. The claims were rejected under the first paragraph of 35 U.S.C. § 112 because they failed to provide a sufficient written description for the large number of peptides currently encompassed by the claim language. As previously set forth, the claims were rejected because of the following issues: 1) The disclosure fails to provide sufficient guidance pertaining to the molecular determinants modulating the CTL-like properties of any given peptide. 2) The disclosure fails to provide sufficient guidance pertaining to acceptable amino acid additions, substitutions, and deletions that will result in retention of the desired HCV CTL epitope. 3) The prior art teaches that single amino acid changes, as well as, the addition or deletion of flanking regions, can influence the immunological properties of any given CTL epitope in an unpredictable manner (Smith *et al.*, 1997; Bertoletti *et al.*, 1994; Johnson *et al.*, 1992; Couillin *et al.*, 1995; and, Hahn *et al.*, 1992; Del Val *et al.*, 1991; Hahn *et al.*, 1992; and, Eisenlohr *et al.*, 1992). 4) The art teaches that the mere presence of an MHC class I binding motif in a peptide is not sufficient to confer binding to the appropriate class I molecule (Nayersina *et al.*,

1993; Bertoletti *et al.*, 1994; Couillin *et al.*, 1995; and, Eisenlohr *et al.*, 1992). 5) The art teaches that the capacity of a putative CTL epitope to bind to a class I molecule does not mean that the epitope will be immunogenic (Nayersina *et al.*, 1993; Couillin *et al.*, 1995; and, Eisenlohr *et al.*, 1992). The rejection was based upon these arguments and the relevant case law, not any particular limitations pertaining to the particular degree of sequence variation claimed.

Applicants alternatively argue that a written description rejection based upon *Lilly* is also inappropriate. This rationale is clearly not supported by the law and arguments set forth *supra*. Several decisions were relied upon in determining whether or not the claim meets the appropriate requirements set forth under the statute. As previously set forth, the written description requirement under Section 112, first paragraph, stipulates that the claimed subject matter must be supported by an adequate written description that is sufficient to enable anyone skilled in the art to make and use the invention. The courts have decided that the specification must demonstrate that the inventor had possession of the claimed invention as of the filing date relied upon. Although the claimed subject matter need not be described identically, nonetheless, the disclosure relied upon must convey to those skilled in the art that applicants had invented the subject matter claimed. *Ralston Purina Company* v. *Far-Mar-Co., Inc.*, 227 U.S.P.Q. 177 (C.A.F.C. 1985). *In re Wilder, et al.*, 222 U.S.P.Q. 369 (C.A.F.C. 1984). *In re Wertheim, et al.*, 191 U.S.P.Q. 90 (C.C.P.A. 1976). *In re Blaser, Germscheid,* and *Worms,* 194 U.S.P.Q. 122 (C.C.P.A. 1977). *In re Driscoll*, 195 U.S.P.Q. 434 (C.C.P.A. 1977). *Utter* v. *Hiraga*, 6 U.S.P.Q.2d 1709 (C.A.F.C. 1988). *University of California* v. *Eli Lilly*, 119 F.3d 1559, 43 U.S.P.Q.2d 1398 (Fed. Cir. 1997). *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18

U.S.P.Q.2d 1016-1031 (C.A.F.C. 1991). *Fiers v. Sugano*, 25 U.S.P.Q.2d 1601-1607 (C.A.F.C. 1993). *In re Bell*, 26 U.S.P.Q.2d 1529-1532 (C.A.F.C. 1993). *In re Deuel*, 34 U.S.P.Q.2d 1210-1216 (C.A.F.C. 1995). Moreover, the courts have decided repeatedly that the inventor must clearly and unambiguously identify the salient characteristics and properties of any given claimed chemical compound, particularly as it applied to nucleic acids and peptides (*University of California* v. *Eli Lilly*, 119 F.3d 1559, 43 U.S.P.Q.2d 1398 (Fed. Cir. 1997); *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 U.S.P.Q.2d 1016-1031 (C.A.F.C. 1991); *Fiers v. Sugano*, 25 U.S.P.Q.2d 1601-1607 (C.A.F.C. 1993); *In re Bell*, 26 U.S.P.Q.2d 1529-1532 (C.A.F.C. 1993); *In re Deuel*, 34 U.S.P.Q.2d 1210-1216 (C.A.F.C. 1995)). Thus, it is not sufficient to simply provide a vague reference to the biological activity of any given amino acid sequence or some generic method of obtaining it.

In the instant application, the claims are directed toward a large genus of compounds. However, as noted in the rejection, considerable unpredictability is present in the art as it pertains to the effects of amino acid replaceability on peptide function. The disclosure merely references a large genus of compounds. However, the specification fails to lead the skilled artisan toward any particular species, other than the specific peptides set forth in the application. Applicants arguments fail to address these concerns. Accordingly, the rejection is hereby proper and maintained.

Non-statutory Double Patenting

5. The non-statutory double patenting rejection, whether of the obviousness-type or non-obviousness-type, is based on a judicially created doctrine grounded in public policy (a policy reflected in

the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent. *In re Thorington,* 418 F.2d 528, 163 U.S.P.Q. 644 (C.C.P.A. 1969); *In re Vogel*, 422 F.2d 438, 164 U.S.P.Q. 619 (C.C.P.A. 1970); *In re Van Ornum*, 686 F.2d 937, 214 U.S.P.Q. 761 (C.C.P.A. 1982); *In re Longi*, 759 F.2d 887, 225 U.S.P.Q. 645 (Fed. Cir. 1985); and *In re Goodman*, 29 U.S.P.Q.2d 2010 (Fed. Cir. 1993).

A timely filed terminal disclaimer in compliance with 37 C.F.R. § 1.321(b) and (c) may be used to overcome an actual or provisional rejection based on a non-statutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 C.F.R. § 1.78(d). Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 C.F.R. § 3.73(b).

6. Claims 67-97 stand rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1 and 11-33 of U.S. Patent No. 5,709,995. Applicants have indicated that a terminal disclaimer was enclosed with the most recent submission. However, perusal of these documents failed to identify the accompanying disclaimer.

Finality of Office Action

7. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. § 1.136(a). **A SHORTENED STATUTORY PERIOD FOR RESPONSE TO THIS FINAL ACTION IS SET TO EXPIRE THREE MONTHS FROM THE DATE OF THIS ACTION. IN THE EVENT A FIRST RESPONSE IS FILED WITHIN TWO MONTHS OF THE MAILING DATE OF THIS FINAL ACTION AND THE ADVISORY ACTION IS NOT MAILED UNTIL AFTER THE END OF THE THREE-MONTH SHORTENED STATUTORY PERIOD, THEN THE**

SHORTENED STATUTORY PERIOD WILL EXPIRE ON THE DATE THE ADVISORY ACTION IS MAILED, AND ANY EXTENSION FEE PURSUANT TO 37 C.F.R. § 1.136(a) WILL BE CALCULATED FROM THE MAILING DATE OF THE ADVISORY ACTION. IN NO EVENT WILL THE STATUTORY PERIOD FOR RESPONSE EXPIRE LATER THAN SIX MONTHS FROM THE DATE OF THIS FINAL ACTION.

Correspondence

8. Correspondence related to this application may be submitted to Group 1600 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Official communications should be directed toward one of the following Group 1600 fax numbers: (703) 308-4242 or (703) 305-3014. Informal communications may be submitted directly to the Examiner through the following fax number: (703) 308-4426. Applicants are encouraged to notify the Examiner prior to the submission of such documents to facilitate their expeditious processing and entry.

9. Any inquiry concerning this communication should be directed to Jeffrey S. Parkin, Ph.D., whose telephone number is (703) 308-2227. The examiner can normally be reached Monday through Thursday from 8:30 AM to 6:00 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner are unsuccessful, the examiner's supervisors, James Housel or Laurie Scheiner, can be reached at (703) 308-4027 or (703) 308-1122, respectively. Any inquiry of a general nature or relating to the status of this application should be directed to the Group 1600 receptionist whose telephone number is (703) 308-0196.

Respectfully,

Jeffrey S. Parkin, Ph.D.
Patent Examiner
Art Unit 1648

HANKYEL T. PARK, PH.D
PRIMARY EXAMINER

03 May, 2003